Serial No.: 09/697,013 Filed: October 25, 2000

Page : 2 of 13

## Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

## Listing of Claims:

## 1-16. (cancelled)

- 17. (Withdrawn) A method for determining a haplotype for ApoE in an individual, comprising genotyping at least two polymorphic sites in ApoE sequence on at least one allele of said individual.
- 18. (Withdrawn) The method of claim 17, wherein at elast one of said polymorphic sites is different from nucleotides 21250 and 21388.
- 19. (Withdrawn) The method of claim 17, wherein said polymorphic sites include at least one site selected from the group consisting of nucleotides 16541, 16767, 16965, 17030, 17098, 17387, 17785, 17874, 17937, 18145, 18476, 19311, 20234, 23524, 23707, 21349, 23759, 23805, and 37237.
- 20. (Withdrawn) The method of claim 19, wherein said genotyping is performed on two alleles of said individual.
- 21. (Withdrawn) The method of claim 19, wherein said genotyping is performed for at least 4 of said polymorphic sites.
- 22. (Withdrawn) The method of claim 19, wherein said genotyping is performed for at least 8 of said polymorphic sites.

Serial No.: 09/697,013 Filed: October 25, 2000

Page : 3 of 13

23. (Withdrawn) The method of claim 19, wherein said genotyping is performed for at least 12 of said polymorphic sites.

- 23. (Withdrawn) The method of claim 19, wherein said genotyping is performed for at least 12 of said polymorphic sites.
- 24. (Withdrawn) The method of claim 19, wherein said genotyping is performed for at least 16 or said polymorphic sites.
- 25: (Withdrawn) The method of claim 19, wherein said genotyping is performed for at least 20 of said polymorphic sites.
- 26. (Withdrawn) A method for classifying ApoE haplotypes for a plurality of individuals, comprising determining at least one ApoE haplotype for each of said plurality of individuals, determining the sequence similarity of said haplotypes; and assigning said haplotypes to groups of haplotypes based on said sequence similarities.
- 27. (Withdrawn) A method for providing an indication of the risk for an individual to develop a disease or condition, comprising determining a haplotype of ApoE in said individual, wherein said haplotype provides a measure of said risk.
- 28. (Withdrawn) The method of claim 27, wherein said disease is selected from the group consisting of coronary heart disease, a non-Alzheimer's Disease neurological disease, Alzheimer's disease, stroke, brain trauma, amyotrophic lateral sclerosis, temporal lobe epilepsy, Wilson's disease, continuous ambulatory peritoneal dialysis, glycogen storage disease type Ia, and age-related macular degeneration.
- 29. (Withdrawn) The method of claim 27, further comprising determining a genotype or haplotype of at least one additional gene, wherein said haplotype of ApoE together with said genotype or haplotype of said at least one additional gene provides a measure of said risk.

Serial No.: 09/697,013

Filed: October 25, 2000

Page : 4 of 13

30. (Withdrawn) A method for diagnosing the presence of a disease in an individual, comprising determining whether said individual has an ApoE haplotype associated with said disease.

- 31. (Withdrawn) The method of claim 30, wherein said disease is selected from the group consisting of coronary heart disease, a non-Alzheimer's Disease neurological disease, Alzheimer's disease, stroke, brain trauma, amytrophic lateral sclerosis, temporal lobe epilepsy, Wilson's disease, continuous ambulatory peritoneal dialysis, glycogen storage disease type Ia, and age-related macular degeneration.
- 32. (Withdrawn) The method of claim 30, further comprising determining a genotype or haplotype of at least one additional gene and determining whether said individual has a combination of said haplotype of ApoE and said genotype or haplotype of said at least one additional gene associated with said disease.
- 33. (Withdrawn) A method for predicting the clinical course for a patient suffering from a disease, comprising determining an ApoE haplotype for said individual, wherein at least one ApoE haplotype is associated with said clinical course.
- 34. (Withdrawn) The method of claim 33, wherein said clinical course comprises a treatment prognosis for a particular method of treatment.
- 35. (Withdrawn) The method of claim 33, wherein said clinical course comprises at least one clinical disease parameter selected from the group consisting of rate of disease development, time interval to death, time interval to dementia, and time interval to inability to live independently.
- 36. (Withdrawn) The method of claim 33, wherein said disease is selected from the group consisting of coronary heart disease, a non-Alzheimer's Disease neurological disease, Alzheimer's disease, stroke, brain trauma, amytrophic lateral sclerosis, temporal lobe epilepsy,

Attorney's Docket No.: 11926-022001 / 0015.UTL1

Applicant: Jeffrey Olson et al. Serial No.: 09/697,013

Filed: October 25, 2000

Page : 5 of 13

Wilson's disease, continuous ambulatory peritoneal dialysis, glycogen storage disease type Ia, and age-related macular degeneration.

- 37. (Withdrawn) The method of claim 33, further comprising determining a genotype or haplotype of at least one additional gene, wherein the combination of said haplotype of ApoE together with said genotype or haplotype of said at least one additional gene is associated with said clinical course.
- 38. (Withdrawn) A method for selecting a subject for prophylactic treatment of a disease, comprising identifying a subject having an ApoE haplotype associated with an elevated risk of developing said disease, wherein said prophylactic treatment can provide a clinical benefit to a said subject.
- 39. (Withdrawn) The method of claim 38, wherein said disease is selected from the group consisting of coronary heart disease, a non-Alzheimer's Disease neurological disease, Alzheimer's disease, stroke, brain trauma, amytrophic lateral sclerosis, temporal lobe epilepsy, Wilson's disease, continuous ambulatory peritoneal dialysis, glycogen storage disease type Ia, and age-related macular degeneration.
- 40. (Withdrawn) The method of claim 38, further comprising determining a genotype or haplotype of at least one additional gene, wherein the combination of said haplotype of ApoE together with said genotype or haplotype of said at least one additional gene is associated with said elevated risk.
- 41. (Withdrawn) A method for selecting a patient for treatment of a disease, comprising determining whether said patient has an ApoE haplotype associated with favorable clinical prognosis with a particular treatment.
- 42. (Withdrawn) The method of claim 41, wherein said disease is selected from the group consisting of coronary heart disease, a non-Alzheimer's Disease neurological disease, Alzheimer's disease, stroke, brain trauma, amytrophic lateral sclerosis, temporal lobe epilepsy,

Serial No.: 09/697,013 Filed: October 25, 2000

Page : 6 of 13

Wilson's disease, continuous ambulatory peritoneal dialysis, glycogen storage disease type Ia, and age-related macular degeneration.

43. (Withdrawn) The method of claim 41, further comprising determining a genotype or haplotype of at least one additional gene, wherein the combination of said haplotype of ApoE together with said genotype or haplotype of said at least one additional gene is associated with said favorable clinical prognosis.

- 44. (Withdrawn) A method for selection of a treatment for a patient suffering from a disease, comprising determining an ApoE haplotype for said patient; and identifying a treatment associated with favorable clinical prognosis for a patient having said ApoE haplotype.
- 45. (Withdrawn) The method of claim 44, wherein said disease is selected from the group consisting of coronary heart disease, a non-Alzheimer's Disease neurological disease, Alzheimer's disease, stroke, brain trauma, amytrophic lateral sclerosis, temporal lobe epilepsy, Wilson's disease, continuous ambulatory peritoneal dialysis, glycogen storage disease type Ia, and age-related macular degeneration.
- 46. (Withdrawn) The method of claim 44, further comprising determining a genotype or haplotype of at least on additional gene, and identifying a treatment associated with favorable clinical prognosis for a patient having the combination of said haplotype of ApoE together with said genotype or haplotype of said at least one additional gene.
  - 47. (Withdrawn) A method of treating a patient suffering from a disease, comprising determining an ApoE haplotype for said patient;

identifying a treatment associated with favorable clinical prognosis for a patient having said ApoE haplotype; and

administering said treatment to said patient.

48. (Withdrawn) The method of claim 47, wherein said disease is selected from the group consisting of coronary heart disease, a non-Alzheimer's Disease neurological disease,

Attorney's Docket No.: 11926-022001 / 0015.UTL1

Applicant: Jeffrey Olson et al. Serial No.: 09/697,013 Filed: October 25, 2000

Page : 7 of 13

Alzheimer's disease, stroke, brain trauma, amytrophic lateral sclerosis, temporal lobe epilepsy, Wilson's disease, continuous ambulatory peritoneal dialysis, glycogen storage disease type Ia, and age-related macular degeneration.

49. (Withdrawn) The method of claim 47, further comprising determining a genotype or haplotype of at least one additional gene;

identifying a treatment associated with favorable clinical prognosis for a patient having the combination of said haplotype of ApoE together with said genotype or haplotype of said at least one additional gene; and

administering said treatment to said patient.

- 50. (Withdrawn) A method for determining whether a biological sample was from an individual, comprising determining the nucleotides present at a plurality of ApoE polymorphic sites in said individual and in DNA obtained from said sample, and determining whether the nucleotides present at said polymorphic sites are the same or different, wherein the presence of the same nucleotides is indicative that said sample is from said individual, and the presence of different nucleotides is indicative that said sample is not from said individual.
- 51. (Withdrawn) The method of claim 50, wherein said plurality of ApoE polymorphic sites comprises an ApoE haplotype.
- 52. (Withdrawn) A method for determining whether an ApoE haplotype is associated with a disease risk comprising

determining ApoE haplotypes for each individual in a set of individuals;
dividing said set of individuals into at least two groups based on ApoE haplotypes; and
determining whether individuals having a particular ApoE haplotype or individuals in a
said group differ from individuals having a different ApoE haplotype or in a different said group

53. (Withdrawn) The method of claim 52, wherein said disease is selected from the group consisting of coronary heart disease, a non-Alzheimer's Disease neurological disease,

in incidence, prevalence, severity, or progression or a combination thereof, of said disease.

Attorney's Docket No.: 11926-022001 / 0015.UTL1

Applicant: Jeffrey Olson et al. Serial No.: 09/697,013

Filed : October 25, 2000

Page : 8 of 13

Alzheimer's disease, stroke, brain trauma, amytrophic lateral sclerosis, temporal lobe epilepsy, Wilson's disease, continuous ambulatory peritoneal dialysis, glycogen storage disease type Ia, and age-related macular degeneration.

54. (Withdrawn) A method for determining whether a combination of an ApoE haplotype and a genotype or haplotype of at least one additional gene is associated with a disease risk, comprising

determining ApoE haplotypes and said genotypes or haplotypes for said at least one additional gene for each individual in a set of individuals;

dividing said set of individuals into at least two groups based on the combinations of ApoE haplotypes and genotype or haplotype of said at least one additional gene; and

determining whether individuals having a particular said combination or individuals in a said group differ from individuals having a different said combination or in a different said group in incidence, prevalence, severity, or progression or a combination thereof, of said disease.

- 55. (Withdrawn) The method of claim 54, wherein said disease is selected from the group consisting of coronary heart disease, a non-Alzheimer's Disease neurological disease, Alzheimer's disease, stroke, brain trauma, amytrophic lateral sclerosis, temporal lobe epilepsy, Wilson's disease, continuous ambulatory peritoneal dialysis, glycogen storage disease type Ia, and age-related macular degeneration.
- 56. (Withdrawn) A method for determining whether an ApoE haplotype is associated with a pharmacologic parameter, comprising measuring said parameter for cells of at least one individual with said ApoE haplotype, measuring said parameter for cells of at least one individual with a different ApoE haplotype, and comparing said measures.
- 57. (newly added) A method for determining whether an individual has a variant nucleotide at a polymorphic site in the ApoE gene, the method comprising
- (a) identifying the nucleotide present at least one of nucleotides 16541, 16747, 16965, 17030, 17098, 17387, 17785, 17937, 18476, 19311, 20234, 21349, 23524, 23707, 23759, and 23805 of SEQ ID NO:5; and

Serial No.: 09/697,013 Filed: October 25, 2000

Page : 9 of 13

(b) determining that the individual has a variant nucleotide at a polymorphic site in the ApoE gene if one or more of the following nucleotides are identified:

```
i) a T at nucleotide 16541 of SEQ ID NO:5;
```

- ii) a T at nucleotide 16747 of SEQ ID NO:5;
- iii) a T at nucleotide 16965 of SEQ ID NO:5;
- iv) a G at nucleotide 17030 of SEQ ID NO:5;
- v) a A at nucleotide 17098 of SEQ ID NO:5;
- vi) a T at nucleotide 17387 of SEQ ID NO:5;
- vii) a T at nucleotide 17785 of SEQ ID NO:5;
- viii) a C at nucleotide 17937 of SEQ ID NO:5;
- ix) a C at nucleotide 18476 of SEQ ID NO:5;
- x) a A at nucleotide 19311 of SEQ ID NO:5;
- xi) a A at nucleotide 20334 of SEQ ID NO:5;
- xii) a T at nucleotide 21349 of SEQ ID NO:5;
- xiii) a A at nucleotide 23524 of SEQ ID NO:5;
- xiv) a A at nucleotide 23707 of SEQ ID NO:5;
- xv) a T at nucleotide 23759 of SEQ ID NO:5; and
- xvi) a G at nucleotide 23805 of SEQ ID NO:5.
- 58. The method of claim 57 further comprising determining the nucleotide present at one or more polymorphic sites selected from: nucleotide 21250 of SEQ ID NO:5; nucleotide 12388 of SEQ ID NO:5; nucleotide 18145 of SEQ ID NO:5; and nucleotide 17874 of SEQ ID NO:5.